

## **REMARKS**

This is a full and timely response to the non-final Office Action mailed by the U.S. Patent and Trademark Office on August 23, 2007. Claims 1-8, 11-18 and 21-23 remain pending in the present application. Claims 1, 11 and 21 are amended. No new matter is introduced. In view of the foregoing amendments and following remarks, reconsideration and allowance of the present application and claims are respectfully requested.

### **Sequence Rules Compliance**

The Office Action states that the application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.82(a)(1) and (a)(2). The Office Action states that such a sequence is present on page 7 of the specification.

In the response filed on August 17, 2004 to the Notice to File Missing Parts of Nonprovisional Application dated June 17, 2004, Applicant amended page 7, lines 7-9 to reduce the hypothetical series of nucleotides to include only eight nucleotides.

Accordingly, Applicant respectfully submits that C.F.R. § 1.82(a)(1) and (a)(2) do not apply to the present application and respectfully request that the requirement for the sequence listing be withdrawn.

### **Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-8, 11-18 and 21-23 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The Office Action states that the terms “inbred population,” “inbred,” and “relatively inbred population” in claims 1, 2, 3, 11, 12, 13, 21, are unclear.

The Office Action also states that the phrases “estimated genotype,” “scores under various assumptions,” and “exhibiting particular homozygous pairs of alleles more frequently than would occur randomly” in claims 1, 11 and 21 are unclear.

The Office Action also states that there is insufficient antecedent basis for the term “the founder” in claims 1, 11 and 21.

With respect to the term “the founder,” Applicant has amended claims 1, 11 and 21 to

recite the term “a founder.”

Inbred population, inbred and relatively inbred population

With respect to the terms “inbred population,” “inbred,” and “relatively inbred population” Applicant respectfully points to the specification, at least on page 3, lines 10-12, which state:

[t]he techniques of the invention are particularly applicable to a population that is relatively inbred and that has a higher occurrence of the genetic disease or trait than a more general population. In such a population, the particular homozygous pairs of alleles that occur more frequently tend to be autozygous alleles descended from a founder of the genetic disease or trait.

Applicant further points to the specification, page 10, lines 1-3, which state:

[i]n FIG. 1, population 1 is relatively inbred compared to a more general population. For example, the Amish population is relatively inbred compared to the general population of the United States or to the general population in regions where the Amish live.

Applicant respectfully submits that after reading Applicant’s specification, one having ordinary skill in the art would understand the terms “inbred population,” “inbred,” and “relatively inbred population” to refer to a population that has a higher occurrence of a genetic disease or trait than a more general population.

Estimated genotype

With respect to the phrase “estimated genotype,” Applicant respectfully points to the specification, page 3, lines 3-8 which state:

[o]ne embodiment of these techniques includes the steps of obtaining actual genotype data for one or more affected people with the genetic disease or trait in a population and/or actual genotype data for their parents, obtaining estimated genotype data for the population, and analyzing the actual and estimated genotype data to find a region in the genome of the affected people that includes markers exhibiting particular homozygous pairs of alleles more frequently than would occur randomly.

Applicant also respectfully points to the specification, page 15, lines 12-22, which state:

[i]n step 32, estimates are obtained of genotype frequency data for the

entire inbred population to which the affected persons and their parents belong. When determining these estimates, it can be assumed that the alleles a child gets for any marker from his or her parents are independent.

In one embodiment, the estimates are found by actually genotyping a subset of the population. An error rate  $e$  for the estimates can be assumed, with the presence of the error indicating that a measured value in the genotyping is a result of a random selection from the population. Standard statistical techniques can be used to determine the error rate  $e$  from the size of the subset and the size of the overall population under consideration. Other techniques can be used to find the estimates without departing from the invention.

Applicant respectfully submits that after reading Applicant's specification, one having ordinary skill in the art would understand the term "estimated genotype" to refer to estimates that are obtained of genotype frequency data for an entire inbred population to which the affected persons and their parents belong.

#### Scores under various assumptions

First, Applicant respectfully points out that the Office Action appears to have taken the phrase "scores under various assumptions" alone and out of context. In claim 1, which is representative of the use of the phrase, the entire phrase reads:

determining a set of scores under various assumptions for each of said markers in said actual and estimated genotype data relative to each person for which actual genotype data was determined with the set of scores for each marker including at least first scores generated to determine probabilities of observing each marker given autozygosity with the a founder and second scores generated to determine probabilities of observing each marker given absence of autozygosity with the founder

Applicant respectfully points to the specification, page 3, line 15 to page 4, line 2, which state:

[i]n one embodiment, analyzing the genotype data further includes the steps of determining scores for each marker in the genotype data relative to each person for which actual genotype data was determined, merging the scores to arrive at a merged score for each marker, and determining a region of markers that has a high run of merged scores.

Preferably, a score for a marker represents a probability that a genotype measured for a person would actually be measured, given some assumption about the autozygosity at each marker's location. This approach results in a

marker receiving a higher score from one form of homozygosity versus another form of homozygosity. The form that receives the higher score tends to be more likely to be associated with the genetic disease or trait.

Applicant respectfully submits that after reading Applicant's specification, one having ordinary skill in the art would understand the term "scores under various assumptions" to refer to determining scores for each marker in the genotype data relative to each person for which actual genotype data was determined, merging the scores to arrive at a merged score for each marker, and determining a region of markers that has a high run of merged scores.

However, in an effort to advance prosecution, Applicant has amended claims 1, 11 and 21 to omit the phrase "under various assumptions."

Exhibiting particular homozygous pairs of alleles more frequently than would occur randomly

With respect to the phrase "exhibiting particular homozygous pairs of alleles more frequently than would occur randomly," Applicant respectfully points to the specification, page 3, lines 3-8 which state:

[o]ne embodiment of these techniques includes the steps of obtaining actual genotype data for one or more affected people with the genetic disease or trait in a population and/or actual genotype data for their parents, obtaining estimated genotype data for the population, and analyzing the actual and estimated genotype data to find a region in the genome of the affected people that includes markers exhibiting particular homozygous pairs of alleles more frequently than would occur randomly.

Applicant also respectfully points to the specification, page 3, lines 10-12 which state:

[t]he techniques of the invention are particularly applicable to a population that is relatively inbred and that has a higher occurrence of the genetic disease or trait than a more general population. In such a population, the particular homozygous pairs of alleles that occur more frequently tend to be autozygous alleles descended from a founder of the genetic disease or trait.

Applicant also respectfully points to the specification, page 12, line 23 to page 13, line 4 which state:

[t]he presence of these markers can be used to help locate a chromosomal region close to alleles causing or otherwise associated with the genetic disease. The overall approach of the invention is to try to find chromosomal regions for people with the disease under study that show a

pattern more consistent than would occur by chance. Part of this pattern is the presence of homozygous alleles that occur more frequently than chance allows. Another part of this pattern is the presence of one type of homozygous alleles more frequently than other types.

Applicant also respectfully points to the specification, page 33, lines 11-12, which state: “[a]ccordingly, particular combinations of homozygous markers that occur more frequently than other combinations of markers are of particular interest.”

Applicant respectfully submits that after reading Applicant’s specification, one having ordinary skill in the art would understand the term “exhibiting particular homozygous pairs of alleles more frequently than would occur randomly” to refer to analyzing the actual and estimated genotype data to find a region in the genome of the affected people that includes markers exhibiting particular homozygous pairs of alleles more frequently than would occur randomly. One having ordinary skill in the art would understand that the overall approach of the invention is to try to find chromosomal regions for people with the disease under study that show a pattern more consistent than would occur by chance and that part of the pattern is the presence of homozygous alleles that occur more frequently than chance allows.

Accordingly, Applicant respectfully submits that claims 1-8, 11-18 and 21-23 are in compliance with 35 U.S.C. § 112, second paragraph, and respectfully request that the rejection be withdrawn.

### **Double Patenting**

Claims 1, 11 and 21 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1, 11 and 21 of copending U.S. Patent Application No. 11/581,132. The Office Action states “although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 11 and 21 of application 11/581132 are a genus of the species claims 1, 11 and 21 in the instant application. The specification of application 11/581132 provides for the species, (see page 17, lines 1-3; page 17, line 18 – page 19, line 3; page 19, line 17 – page 21, line 6).”

Applicant submits herewith a terminal disclaimer, disclaiming the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of any patent granted on U.S. Application No.

11/581,132.

Accordingly, Applicant respectfully requests that the obviousness-type double patenting rejection be withdrawn.

**CONCLUSION**

For at least the foregoing reasons, Applicant respectfully requests that all outstanding rejections be withdrawn and that all pending claims of this application be allowed to issue. If the Examiner has any comments regarding Applicant's response or intends to dispose of this matter in a manner other than a notice of allowance, Applicant requests that the Examiner telephone Applicant's undersigned attorney.

Respectfully submitted,

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